


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT-7945	FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/IT2004/000014	International filing date (day/month/year) 23.01.2004	Priority date (day/month/year) 10.02.2003
International Patent Classification (IPC) or national classification and IPC A61K31/205, A61K31/17, A61P3/10		
Applicant SIGMA-TAU INDUSTRIE FARMACEUTICHE...et al		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand 04.08.2004	Date of completion of this report 11.03.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer A. Jakobs Telephone No. +31 70 340-2617	



Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-22 as originally filed

Claims, Numbers

1-16 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
 4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 2

because:

☒ the said international application, or the said claims Nos. 2 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-16
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-16
Industrial applicability (IA)	Yes: Claims	See separate sheet
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

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Re Item III.

Claim 2 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

No International Preliminary Examination will be carried out in respect of subject matter which is not covered by the search report (Rule 66.1 (e) PCT).

Re Item V.

1. The following documents are referred to in this communication:

- D1: WO 99/59957 A (TINTI MARIA ORNELLA ; MARZI MAURO (IT); ARDUINI ARDUINO (IT); CHIODI P) 25 November 1999 (1999-11-25)
- D2: GIANNESI, FABIO ET AL: "Discovery of a Long-Chain Carbamoyl Aminocarnitine Derivative, a Reversible Carnitine Palmitoyltransferase Inhibitor with Antiketotic and Antidiabetic Activity" JOURNAL OF MEDICINAL CHEMISTRY , 46(2), 303-309 CODEN: JMCMAR; ISSN: 0022-2623, 2003, XP002281384
- D3: DAGOGO-JACK S ET AL: "PATHOPHYSIOLOGY OF TYPE 2 DIABETES AND MODES OF ACTION OF THERAPEUTIC INTERVENTIONS" ARCHIVES OF INTERNAL MEDICINE, AMERICAN MEDICAL ASSOCIATION, CHICAGO, IL, US, vol. 157, no. 16, 8 September 1997 (1997-09-08), pages 1802-1817, XP000872498 ISSN: 0003-9926

2. The subject matter of claims 1-16 relates to compositions or substances in a method of treatment/method of diagnosis of the human or animal body. For the assessment of the present claims 1-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such

a compound for the manufacture of a medicament for a new medical treatment.

3. INDEPENDENT CLAIM 1

2.1. The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claim 1 does not involve an inventive step in the sense of Article 33(3)PCT.

3.1.1.

Document D1, which is considered to represent the most relevant state of the art to the subject matter of claim 1, discloses (see the passages cited in the search report) pharmaceutical compositions comprising R-4-trimethylammonium-3-(tetradecylcarbamoyl)-amino butyrate (ST 1326), and its use as antidiabetic. Said compound may be used either alone or in combination with other antidiabetic agents including biguanides.

3.1.2.

Document D2, discloses (see the passages cited in the search report) pharmaceutical compositions comprising R-4-trimethylammonium-3-(tetradecylcarbamoyl)-amino butyrate (compound 17), and that compound 17 has been selected as a potential antidiabetic drug.

3.1.2

The subject-matter of independent claim 1 differs from the disclosure of D1 in that (see the passages cited in the search report): metformin is used as the additional biguanide antidiabetic agent.

3.1.3

The problem to be solved by the present invention may therefore be regarded as the provision of an improved treatment of diabetes and pharmaceutical compositions comprising the active ingredients.

3.1.4

In view of D3 the solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
- According to D3, Metformin alone or carnitine palmitoyltransferase I inhibitors alone,

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or Metformin in combination with other antidiabetic agents may achieve an additive or synergistic effect and thereby improve glycemic control in type 2 Diabetes.

- Furthermore, the use of a combination of two agents known to be active in relation to the treatment of a particular disorder (here Diabetes), can not, in the absence of a special technical effect, be considered to be inventive. D3 discloses that "One promising strategy is an attack on multiple pathophysiological processes by combining antidiabetic agents with disparate mechanisms of action".

3.1.5

Therefore the features disclosed in D1 (or D2) and D3 would be combined by the skilled person, without exercise of any inventive skills in order to solve the problem posed. The proposed solution in independent claim 1 thus cannot be considered inventive (Article 33(3) PCT).

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DEPENDENT CLAIMS 2-16

Dependent claims 2-16 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT).